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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,320	06/02/2005	Akihiro Tada	TOYA107.007APC	3197

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EXAMINER

SZNAIDMAN, MARCOS L

ART UNIT	PAPER NUMBER
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1628

NOTIFICATION DATE	DELIVERY MODE
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10/04/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
efiling@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No. 10/537,320	Applicant(s) TADA ET AL.	
	Examiner MARCOS SZNAIDMAN	Art Unit 1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 June 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7, 12-14, 16 and 17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7, 12-14, 16 and 17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is in response to applicant's request for continued examination filed on June 28, 2010.

Receipt of Declarations under 37 CFR 1.132 is acknowledged.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Status of Claims

Claims 7, 12-14 and 16-17 are currently pending and are the subject of this office action.

Claims 7, 12-14 and 16-17 are presently under examination.

Priority

The present application is a 371 of PCT/JP03/15267 filed on 11/28/2003, and claims priority to foreign application JAPAN 2002-350733 filed on 12/03/2002.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a certified English translation of the

Art Unit: 1628

foreign application must be submitted in reply to this action. 37 CFR 41.154(b) and 41.202(e).

Failure to provide a certified translation may result in no benefit being accorded for the non-English application.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103 (Maintained Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

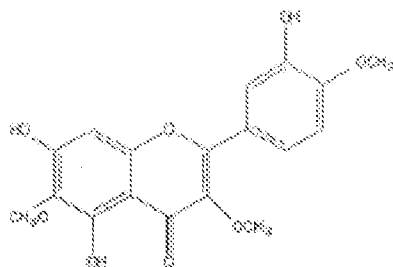
Art Unit: 1628

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

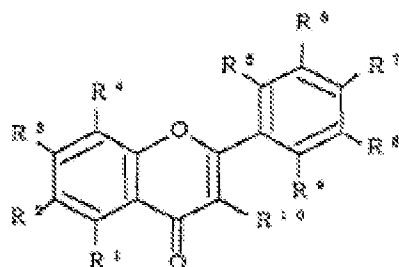
Claims 7, 12-14 and 16-17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ishida et. al. (EP 1147764, cited by applicant, cited in prior office action).

Claim 7 recite a method for whitening the skin comprising: a step of applying Centaureidin represented by the following formula:



and/or a salty thereof to the skin of an individual in need of skin whitening, whereby elongation of melanocytic dendrites is inhibited.

For claim 7, Ishida et. al. teach a cosmetic composition of general formula I (see page 3):



, having a sufficient whitening effect, a so called anti skin-aging effect as vitalizing the skin and preventing wrinkles (see page 2, paragraphs [0006] and [0007]). Ishida does not specifically disclose the compound centaureidin. Ishida et. al. limit their structure to at least four methoxy groups (see page 3, line 18), while Centaureidin has three methoxy groups.

However, MPEP 2144, Section III states: prior art structures do not have to be true homologs or isomers to render structurally similar compounds *prima facie* obvious. *In re Payne*, 606 F.2d 303, 203 USPQ 245 (CCPA 1979) (Claimed and prior art

Art Unit: 1628

compounds were both directed to heterocyclic carbamoyloximino compounds having pesticidal activity. The only structural difference between the claimed and prior art was that the ring structures of the claimed compounds had two carbon atoms between two sulfur atoms, whereas the prior art ring structures had either one or three carbon atoms between two sulfur atoms. The court held that although the prior art compounds were not true homologs or isomers of the claimed compounds, the similarity between the chemical structures and properties is sufficiently close that one of ordinary skill in the art would have been motivated to make the claimed compounds in searching for new pesticides). In *re Gyurik*, 201 USPQ 552, 596 F2d 1012 on page 557 states: “In obviousness rejections based on close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the *prima facie* case of obviousness, rises from the expectation that compounds similar in structure will have similar properties.” In this case, it is expected that compounds of general structure I taught by Ishida et. al. and Centaureidin of the instant application, differing by only one –CH₃ group, would have similar chemical, physical and biochemical properties.

The phrase: “whereby elongation of melanocytic dendrites is inhibited” is not given any patentable weight because: the whereby clause represents the intended result of the process steps positively recited. See MPEP 2111.04: In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a “whereby” clause states a condition that is material to patentability; it cannot be ignored in order to change the substance of the invention.” *Id.* However, the court noted (quoting *Minton v. Nat ’l Ass ’n of Securities Dealers, Inc.*, 336

Art Unit: 1628

F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a “whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.” *Id.*

Alternatively, even if one were to give some weight to the phrase: “whereby elongation of melanocytic dendrites is inhibited”, naturally flows from the teachings of the prior art and will necessary be present in the method made obvious by Ishida, since Ishida teaches the same active steps of the instant application: applying Centaureidin to the skin of individuals in need of of skin whitening. In other words, products of identical or similar composition cannot exert mutually exclusive properties when administered under the same circumstances. MPEP 2112 I states: “The discovery of a previously unappreciated property of a prior art composition or a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer”.

Since Ishida et. al. teach a method of skin whitening with compounds of formula I (see above), and since centaureidin, which differs from those compounds by just one methyl group is expected to have similar chemical and biological properties, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any compound of formula I or structurally related to formula I) for another (centaureidin) with an expectation of success, since the prior art establishes that both function in similar manner, thus resulting in the practice of claim 7, with a reasonable expectation of success.

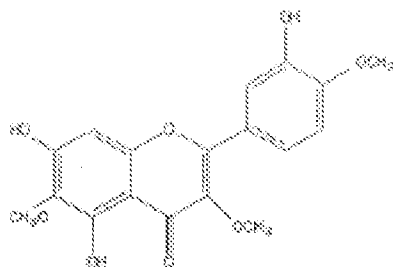
Claim 12 is a narrower version of claim 7, which insofar recites the same limitations as claim 7, wherein a skin preparation for external use comprising 0.005 to 5% by weight of Centaureidin is applied.

Claim 13, further limits claim 12, wherein the skin preparation for external use is a cosmetic.

For claims 12 and 13, Ishida further teaches: that the cosmetic composition (cosmetic compositions are for external use) of the present invention includes 0.00005 to 10% by weight of the compounds of formula I (see page 2, paragraph [0007]). These percentages clearly overlap with the percentages of the instant claims.

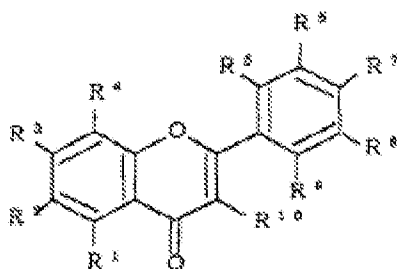
Ishida does not teach the exact same percentages of the instant claims. However, MPEP 2144.05 states: In the case where the claimed ranges “overlap or lie inside ranges disclosed by the prior art” a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Thus resulting in the practice of claims 12-13 with a reasonable expectation of success.

Claim 14 recites a method for treating dyschromatosis (a skin disease in which individuals have anomalous skin pigmentation) comprising: a step of applying Centaureidin represented by the following formula:



and/or a salty thereof to the skin of an individual in need of skin whitening, whereby elongation of melanocytic dendrites is inhibited.

For claims 14 , Ishida et. al. teach a cosmetic composition of general formula I (see page 3):



, having a sufficient whitening effect, a so called anti skin-aging effect as vitalizing the skin and preventing wrinkles (see page 2, paragraphs [0006] and [0007]). Ishida does not specifically disclose the compound centaureidin (Ishida et. al. limit their structure to at least four methoxy groups (see page 3, line 18), while Centaureidin has three methoxy groups) or the specific treatment of dyschromatosis

However, MPEP 2144, Section III states: prior art structures do not have to be true homologs or isomers to render structurally similar compounds *prima facie* obvious.

In re Payne, 606 F.2d 303, 203 USPQ 245 (CCPA 1979) (Claimed and prior art

Art Unit: 1628

compounds were both directed to heterocyclic carbamoyloximino compounds having pesticidal activity. The only structural difference between the claimed and prior art was that the ring structures of the claimed compounds had two carbon atoms between two sulfur atoms, whereas the prior art ring structures had either one or three carbon atoms between two sulfur atoms. The court held that although the prior art compounds were not true homologs or isomers of the claimed compounds, the similarity between the chemical structures and properties is sufficiently close that one of ordinary skill in the art would have been motivated to make the claimed compounds in searching for new pesticides). In *re Gyurik*, 201 USPQ 552, 596 F2d 1012 on page 557 states: “In obviousness rejections based on close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the *prima facie* case of obviousness, rises from the expectation that compounds similar in structure will have similar properties.” In this case, it is expected that compounds of general structure I taught by Ishida et. al. and Centaureidin of the instant application, differing by only one –CH₃ group, would have similar chemical, physical and biochemical properties.

The phrase: “whereby elongation of melanocytic dendrites is inhibited” is not given any patentable weight because: the whereby clause represents the intended result of the process steps positively recited. See MPEP 2111.04: In *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005), the court held that when a “whereby” clause states a condition that is material to patentability; it cannot be ignored in order to change the substance of the invention.” *Id.* However, the court noted (quoting *Minton v. Nat ’l Ass ’n of Securities Dealers, Inc.*, 336

Art Unit: 1628

F.3d 1373, 1381, 67 USPQ2d 1614, 1620 (Fed. Cir. 2003)) that a “whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.” *Id.*

Alternatively, even if one were to give some weight to the phrase: “whereby elongation of melanocytic dendrites is inhibited”, naturally flows from the teachings of the prior art, and will necessary be present in the method made obvious by Ishida, since Ishida teaches the same active steps of the instant application: applying Centaureidin to the skin of individuals of skin whitening. In other words, products of identical or similar composition cannot exert mutually exclusive properties when administered under the same circumstances. MPEP 2112 I states: “The discovery of a previously unappreciated property of a prior art composition or a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer”.

Since Ishida et. al. teach a method of skin whitening with compounds of formula I (see above), and since dyschromatosis is a disease associated with anomalous darkening of the skin, and since centaureidin, which differs from those compounds by just one methyl group is expected to have similar chemical and biological properties, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any compound of formula I or structurally related to formula I) for another (centaureidin) with an expectation of success, since the prior art establishes that both function in similar manner, thus resulting in the practice of claims 14, with a reasonable expectation of success.

Claim 16 is a narrower version of claim 14, which insofar recites the same limitations as claim 14, wherein a skin preparation for external use comprising 0.005 to 5% by weight of Centaureidin is applied.

Claim 17, further limits claim 16, wherein the skin preparation for external use is a cosmetic.

For claims 16 and 17, Ishida further teaches: that the cosmetic composition (cosmetic compositions are for external use) of the present invention includes 0.00005 to 10% by weight of the compounds of formula I (see page 2, paragraph [0007]). These percentages clearly overlap with the percentages of the instant claims.

Ishida does not teach the exact same percentages of the instant claims. However, MPEP 2144.05 states: In the case where the claimed ranges “overlap or lie inside ranges disclosed by the prior art” a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Thus resulting in the practice of claims 16-17 with a reasonable expectation of success.

Response to Applicant's arguments related to the above rejection

Applicant's arguments have been fully considered but are not persuasive.

Applicant argues that:

Centaureidin differs from any of the compounds disclosed by the prior art, for example nobiletin in the mechanism of action. Again, the current 1.132 declaration by

Art Unit: 1628

Dr. Tada shows that nobieltin inhibits production of melanin, however, centaureidin does not. In a previous 1.132 declaration (04/22/09) Dr. Tada was also able to demonstrate that centaureidin inhibits elongation of dendrites, while nobieltin does not. As such the compounds of the prior art and the instant application have completely different properties.

Examiner's response:

As discussed in previous office actions: the prior art teaches that similar compounds are effective in treating the same disease (skin darkening) in the same population (patients with skin decoloration), as such it would have been expected that the same or structurally similar compounds (i.e. the compounds disclosed by Ishida and centaureidin) will have the same or similar effect regardless of their mechanism of action. Applicant was not able to show any unexpected result for centaureidin when compared with the compounds disclosed by Ishida. Applicant simply discovered that centaureidin has a completely different mechanism of action than the compounds disclosed by Ishida. However, since the mechanism of action does not translate in any effective difference in pharmacological behavior (both compounds are effective in treating skin darkening), the difference in mechanism of action becomes irrelevant, since the skill in the art will observe that the structure of centaureidin is very similar to the structure of the compounds disclosed by Ishida, and as such expect to have similar pharmacological properties (i.e. skin whitening) even if achieves the same result through a different mechanism of action.

Conclusion

No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1628

Application/Control Number: 10/537,320

Page 15

Art Unit: 1628

September 23, 2010.